Fact Sheet

Defense Advanced Research Projects Agency

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DARPA and Accelerating Critical Therapeutics

DARPA has a long-standing research program to protect warfighters from infectious diseases encountered during deployments. Current research activities include development of new, rapid mechanisms to discover, test and manufacture large quantities of critical therapeutics.

In response to emerging and novel biologic threats, DARPA's Accelerated Manufacture of Pharmaceuticals (AMP) program started in 2005. AMP focuses on identifying, developing and demonstrating new ways to produce large amounts of pharmaceuticals, such as high-quality vaccine-grade protein within three months of sequencing the pathogen DNA. Inspiration for this scalable approach is a preparedness strategy that provides capability to respond quickly to emerging biothreats.

In response to the 2009 H1N1 swine flu pandemic, AMP's plant-based platform redirected its rapid scale-up processes that were initially developed for avian influenza. After receiving the H1N1 DNA sequence April 29, a candidate recombinant H1 protein, an essential component of a vaccine, was produced within four weeks.

AMP's plant-based system combines three major components to rapidly express vaccine candidate proteins: non-genetically modified plant seedlings, viral-based protein expression vectors and vacuum infiltration/viral infection methodologies. Upon receipt of the gene sequence for a target protein, that sequence is cloned into a viral-based protein expression vector. This virus vector provides the mechanism for transferring millions of copies of the target gene

sequence into the plant cells. Upon transfer to the plant, the virus replicates the target gene and stimulates protein expression in those plants.

Essentially, this platform uses the plant's protein synthesis capabilities to produce the specific recombinant protein material that will be the active component of a vaccine. Scale-up could be as simple as infiltrating additional non-genetically modified seedlings. Compared to other vaccine technologies, this platform's production time allows for protein expression, the first step in vaccine production, in less than five weeks.

DARPA is pursuing this technology development along two, parallel paths:

1) A pilot facility to produce a vaccine-grade recombinant protein under current good manufacturing practices (cGMP) for formulation, immunogenicity and toxicology studies. Data along with results from those studies will lead to filing of an investigational new drug package with the FDA allowing the start of a phase 1 clinical trial. The data generated would be needed to approve this approach for rapid, flexible vaccine manufacturing under an emergency use authorization scenario.
2) Demonstrate a proof-of-concept capability for cGMP scale up of the plant-based platform to 10 million doses per month.

Because of the time required to address key FDA regulatory requirements, this program is not anticipated to deliver H1N1 vaccine for widespread human use during the 2010 flu season. Protein produced in a facility that meets FDA requirements, is formulated into a vaccine and has completed phase 1 clinical studies has a higher chance of being authorized by the FDA for use in a public health emergency under an emergency use authorization.